## Blood and Beyond

Sanquin Blood Supply is responsible for safe and efficient blood supply in the Netherlands on a not-for-profit basis. Sanquin also develops and produces pharmaceutical products, conducts high-quality scientific research, and develops and performs a multitude of diagnostic services. Continuous research and innovation lead to new and improved products and services. Quality and development therefore go hand in hand.

## Sanquin Divisions

Blood Bank
Diagnostic Services
Plasma Products
Research
Reagents
Pharmaceutical Services


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Sanquin
Blood Supply

# LABORATORY FOR CELL THERAPY

Your experienced partner in translational research

RESEARCH | DIAGNOSTICS | PHARMACEUTICALS

# LABORATORY FOR CELL THERAPY

The Laboratory for Cell Therapy started its activities in 1979 and is now part of Sanquin Blood Supply Foundation. The Laboratory is positioned within Sanquin's Research division to benefit optimally from the scientific environment. All research within this division is related to the many aspects of blood, blood transfusion and immunology. The division employs around 300 scientists. The Laboratory for Cell Therapy serves both academic and non-academic hospitals as well as commercial partners and is actively involved in the development of new cellular products for cell therapy.

*"Our GMP facility for cellular therapy is instrumental to translate concepts coming from innovative, basic research into the clinical practice."*

*René A.W. van Lier, Research Director Sanquin Blood Supply*

### Sanquin Blood Supply provides the full chain for production of a cellular product

We take care of collection of blood cells by aphaeresis procedure and GMP manufacturing of the cellular product, both Advanced Therapy Medicinal Products (ATMP) and non-ATMP, such as stem cell products and therapeutic T-cells. We provide quality control, storage and delivery of the cellular product.

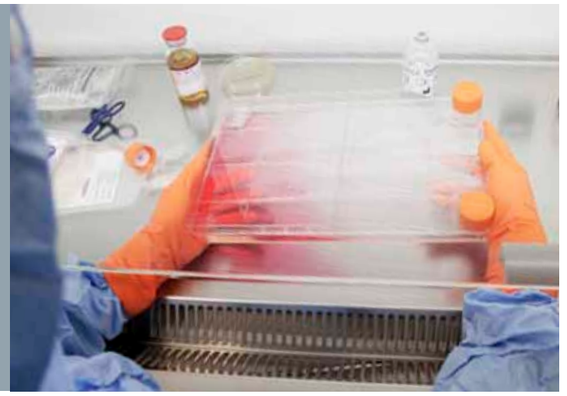
### The Laboratory for Cell Therapy facilitates bench-to-bedside development of novel cellular therapies

We translate cell therapy protocols from the lab to the clinic. Our services range from the technical level to the submission of clinical protocols and Investigational Medical Product Dossier.

**Our state-of-the-art facility** covers 275 square meters including classes B, C (Classes 10,000 / 100,000) and MLII cleanrooms, a QC laboratory and cryopreservation area.

*"Thanks to our long standing successful collaboration, we have developed a well-oiled Sanquin-AMC stem cell transplantation team"*

*Rien van Oers, Head of Department of Haematology, Academic Medical Center Amsterdam*



# Our products

## Non-ATMP

### Stem cell products

Hematopoietic stem cell (HSC) transplantation is the procedure to replace stem and progenitor cells that have been destroyed by high doses of chemotherapy and/or radiation therapy. The stem cells can be derived from bone marrow, peripheral blood or umbilical cord blood and used for autologous or allogeneic purposes. Within the Laboratory for Cell Therapy, blood and bone marrow is processed and cryopreserved for patients who are in need of stem cell transplantation. Besides hematological recovery, HSCs are also used for other applications such as for the treatment of Crohn's disease, acute myocard infarction or chronic peripheral artery disease.

### Therapeutic T cells

Patients who suffer from a relapse after stem cell transplantation can be treated with a donor lymphocyte infusion (DLI). With this procedure the lymphocytes from the original donor are infused after the transplantation to augment the anti-tumor response or to ensure that the donor stem cells remain engrafted.

## ATMP

### Mesenchymal stromal cells

Mesenchymal stromal cells (MSC) are a heterogenous population of multi-potent cells that have the ability to migrate to sites of inflammation and injury and display immunomodulatory capacities. Clinical applications of MSC include treatment of therapy resistant acute graft versus host disease (GvHD), rejection after hematopoietic stem cell or solid organ transplantation and refractory Crohn's disease. A clinical grade MSC expansion protocol has been developed to generate a standardized bone marrow-derived MSC product from third-party donors.

### Tumor-infiltrating lymphocytes

Tumors from patients with advanced melanoma contain tumor-infiltrating lymphocytes (TIL) with anti-tumor reactivity targeting a variety of melanoma-associated antigens. These TIL can be expanded at large scale in vitro and are now tested for treatment of advanced melanoma in a randomized phase II study at the Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital (NKI-AvL). In collaboration with Prof John Haanen and Prof Ton Schumacher of the Department of Immunology NKI-AvL, The Laboratory for Cell Therapy will actively participate in the generation of TIL and optimization of the TIL protocol for future clinical studies.

### Dendritic Cells

Dendritic cells (DCs) are the best antigen presenting cells in the human body and are involved in activation of the adoptive immune response. DCs can be cultured ex vivo from autologous monocytes and subsequently used as immunotherapy. Recently we have developed a method to generate clinical grade immuno-activatory DCs that will be studied in a phase I clinical study in the Academic Medical Center Amsterdam for patients suffering from oesophageal adeno-carcinoma. In situations where the immune response is non-beneficial or unwanted, such as transplantation rejections and auto-immunity, tolerogenic DCs can be used to suppress the immune system. In cooperation with the Department of Immunopathology we are currently studying if these tolerogenic DCs may also have a clinical application.

## Accreditation

The Laboratory for Cell Therapy is ISO-9001, ISO-13485 and ISO 14971 certified since 2004 and is acknowledged by the Dutch Ministry of health as a tissue bank according to EU directive 2004/23/EC. In June 2007 the laboratory obtained JACIE accreditation which was prolonged in 2010 until June 2014. Published in December 2007, the EU directive EC/1394/2007 defines somatic cell therapy, gene therapy and tissue engineering as “Advanced Therapies” which are now classified as medicinal products (Advanced Therapy Medicinal Products, ATMPs) for which a Manufacturing license is required. Directive 2001/83/EC describes all aspects concerning manufacturing human medicinal products and is complemented by the EU GMP guide which describes all aspects of Good Manufacturing Practice.

*“We aim to develop novel cellular products that meet the needs of our customers and comply with the highest standards”*

*Daphne Thijssen-Timmer, project leader Cellular Therapies, Sanquin Blood Supply*

### Techniques

- Preparation of (stem) cell products
- Magnetic cell sorting using CliniMACS
- Generation of ATMPs
- Cell banking
- Thawing of cellular products for clinical use
- Progenitor cell assays
- Quality control assays

### Equipment

- Cobe 2991 cell processor (Gambro-BCT)
- CliniMACS®
- Planer® freezers
- Gene pulser Xcell Electroporation system
- Leica DM IL LED microscopes

## Key publications


Boks,M.A., Kager-Groenland,J.R., Haasjes,M.S., Zwaginga,J.J., van Ham,S.M., & ten Brinke, A. (2012) IL-10-generated tolerogenic dendritic cells are optimal for functional regulatory T cell induction--a comparative study of human clinical-applicable DC. Clin.Immunol. 142, 332-342.

Hommes,D.W., Duijvestein,M., Zelinkova,Z., Stokkers,P.C., Ley,M.H., Stoker,J., Voermans,C., van Oers,M.H., & Kersten,M.J. (2011) Long-term follow-up of autologous hematopoietic stem cell transplantation for severe refractory Crohn’s disease. J.Crohns.Colitis. 5, 543-549.

ten Brinke, A., van,S.G., Visser,R., de Gruijl,T.D., Zwaginga, J.J., & van Ham, S.M. (2010) Monophosphoryl lipid A plus IFNgamma maturation of dendritic cells induces antigen-specific CD8+ cytotoxic T cells with high cytolytic potential. Cancer Immunol Immunother. 59, 1185-1195.

Tijssen,M.R., van Hennik,P.B., Di,S.F., Zwaginga,J.J., van der Schoot,C.E., & Voermans,C. (2008) Transplantation of human peripheral blood CD34-positive cells in combination with ex vivo generated megakaryocytes results in fast platelet formation in NOD/SCID mice. Leukemia 22, 203-208.


*“This new facility, with its dedicated technical staff, provides the optimal infrastructure to translate novel cell therapy protocols from bench to bedside”*

*Carlijn Voermans, Head of Laboratory for Cell Therapy*


Tijssen,M.R., Woelders,H., de Vries-van,R.A., van der Schoot,C.E., Voermans,C., & Lagerberg,J.W. (2008) Improved postthaw viability and in vitro functionality of peripheral blood hematopoietic progenitor cells after cryopreservation with a theoretically optimized freezing curve. Transfusion 48, 893-901.

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van Beem RT, Hirsch A, Lommerse IM, Zwaginga JJ, Noort WA, Biemond BJ, Piek JJ, van der Schoot CE, Voermans C. (2008) Recovery and functional activity of mononuclear bone marrow and peripheral blood cells after different cell isolation protocols used in clinical trials for cell therapy after acute myocardial infarction. EuroIntervention 4 133-8.


### Contact

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